REMARKS

The Office Action of January 19, 2007 presents the examination of claims 2-8 and 11-15, claims 1, 9 and 10 being withdrawn as a result of a Restriction Requirement.

Claim 2 is amended to recite the term "isolated", as recommended by the Examiner, and to incorporate the features of claim 4. Claim 5 is amended as to dependency. Claim 6 is amended as to dependency and to incorporate the features of claim 8. Claim 7 is amended to recite particular sequences as set forth in the Sequence Listing. Claim 9 (directed to a second species) is amended as to dependency and to incorporate the features of claim 10.

Claims 11 and 12 are amended as to dependency and to recite further features of a pharmaceutical composition.

Claims 1, 4, 8 and 10 are canceled. Applicants reserve the right to file an application directed to the canceled subject matter pursuant to 35 USC § 120.

Restriction Requirement

The Examiner has improperly restricted the claims of the present application; she incorrectly deems each particular sequence to require a separate search of the prior art. The claims require a peptide having an amino acid sequence that is at least a part of the protein described by SEQ ID NO: 2. The individual species recited a SEQ ID NOS: 3-52 are portions of the peptide sequence of SEQ ID NO: 2 that represent particularized embodiments of the invention. See, for instance, Example 8 delineating the portions of SEQ ID NO: 2 represented by SEQ ID NOS: 25-29. Applicants submit that a search of SEQ ID NO: 2 will reveal the prior art relevant to the present invention.

Should the presently elected species be found patentable over the prior art, the Examiner is requested to select another species for examination, to determine if the generic claim 2 is patentable.

Priority claim

A verified translation of the priority document is attached hereto. The priority date of the present application is therefore established as August 28, 1998 as originally claimed.

Rejection under 35 USC § 101

Claims 2-8 and 11-15 are rejected under 35 USC § 101 as being non-statutory subject matter, in particular, being natural products. The claims are amended to recite that the peptide is one that is "isolated", as recommended by the Examiner. Thus, the instant rejection is obviated.

Rejection under 35 USC § 112, second paragraph

Claims 12-13 and 15 are rejected under 35 USC § 112, second paragraph, as allegedly being vague and indefinite. The Examiner indicates that there is insufficient antecedent basis in the base claims for the term "any one of the DNAs that encode...". The indefinite article "a" is now used, thus overcoming this rejection.

Rejection under 35 USC § 112, first paragraph

Claims 2-8 and 11-15 are rejected under 35 USC § 112, first paragraph for alleged lack of adequate written description support by the specification. This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested.

The Examiner asserts that the claims are unduly broad. This is first and foremost because the Examiner is unreasonably interpreting the claims. For instance, she asserts that "an amino acid sequence of SEQ ID NO: 3" can be as short as two amino acids. (See, page 4 of the Office Action.) This is a wholly unreasonable interpretation, because as the Examiner also notes, the claim recites "comprising an amino acid sequence according to claim 3." Thus, the entirety of the amino acid sequence of claim 3 must be included in the claimed peptide.

The Examiner also asserts that the claims encompass peptides of significantly diverse function. However, as claimed, the peptides must have the function of binding to an HLA-A24 or HLA-A3 antigen and be recognized by CTL. Thus, the function that the peptides must exhibit is recited in the claims.

Finally, the Examiner asserts that the specification does not provide any description of structure that is required for function. This is simply untrue. The specification includes SEQ ID NO: 2, from which all of the peptides of the presently claimed invention are derived. The specification further specifies particular portions of SEQ ID NO: 2 that represent embodiments of the invention (at least by SEQ ID NO) and also describes specific variations of SEQ ID NO: 2 that are included in the invention. The Examiner is just wrong on this point.

Furthermore, one of ordinary skill in the art can understand, even in the absence of specific experimental results, those peptides having the requisite "motifs" bind to an HLA antigen.

As to claim 2, the claimed subject matter is a recombinant polypeptide produced by a process expressing a DNA encoding a tumor antigen peptide(s) or a derivative(s) as claimed in Claims 2, 3, 5, 6, 7 or 9. Specifically, the recombinant polypeptide comprises at least one of partial peptides shown in SEQ ID NO: 3-52 or derivatives thereof, which partial peptides have 8-11 amino acid sequences derived from SEQ ID NO: 2.

The fact that the protein consisting of the amino acid sequence of SEQ ID NO: 2 indeed

functions as a tumor antigen protein is shown in working Examples 1 and 2. That is, KE-4CTL reacted more strongly to VA-13 doubly transfected with HLA-A2402 and clone 13, and produced more IFN-γ than to VA-13 transfected with only HLA-A2402.

The state of the art at the time the invention was made was such that there are certain rules (motifs) in the sequences of antigen peptides that bind to and presented by HLA antigens. Regarding the motif for HLA-A24, it had been known that, in the sequence of peptides consisting of 8 to 11 amino acids, the amino acid at position 2 is Tyr, Phe, Met, or Trp, and the amino acid at the C-terminus is Phe, Leu, Ile, Trp or Met (J. Immunol., 152:3913, 1994; Immunogenetics, 41: 178, 1995; J. Immunol., 155:4307, 1994). Regarding the motif for HLA-A2, it had been known that, in the sequence of peptides consisting of 8-11 amino acids, the amino acid at position 2 and the one at the C-terminus are in any one of combinations shown in Table 1 at page 21 (Immunogenetics, 41:178, 1995; J. Immunol, 155:p.4749, 1995). Further, one ordinary skilled in the art can identify a partial peptide having a sequence corresponding to any one of SEQ ID NOs: 3-52 using the NIH BIMAS soft (http://www-bimas.dcrt.nih.gov/molbio/hla_bind/). (References cited are all of record).

As demonstrated in Example 4, peptides of SEQ ID NOs: 3-9 have the IFN-γ inducing activity. Example 6 demonstrates that peptides of SEQ ID NOs: 3 and 6 have an activity of inducing antigen-specific CTLs. Further, Example 8 demonstrates that peptides of SEQ ID NOs: 25-29 have IFN-γ -inducing activity.

It is well known in the art that peptide derivatives prepared from a partial peptide having a motif as an HLA protein binding antigen through the substitution of an amino acid(s) at position 2 and/or C-terminus have the same activity as the partial peptide. Therefore, peptide derivatives prepared from partial peptides of 8-11 amino acids having an HLA-A24 motif through the substitution of position 2 amino acid with Phe, Leu, Ile, Trp or Met, and/or substitution of C-terminal amino acid with Phe, Leu, Ile, Trp or Met will be expected to bind HLA-A24 antigen.

Further, peptide derivatives prepared from partial peptides of 8-11 amino acids having an HLA-A2 motif through the substitution of position 2 and/or C-terminal amino acid according to the teaching in Table 1 at page 21 of the present specification would be expected to be operable embodiments.

Claims 2-8 and 11-15 are rejected under 35 USC § 112, first paragraph also for alleged lack of enablement of the scope of the claims. Once again, the Examiner asserts an unreasonable claim interpretation that the claims encompass sequences as short as two amino acids. This is unreasonable from two standpoints. First, as explained above, the claims "comprise" peptides of sequences much longer than two amino acids. Second, the claims recite that the peptides are bound by HLA antigens, and the skilled artisan, to whom the specification is addressed, recognizes that HLA binding domains are at least six amino acids in length.

The Examiner's interpretation of Example 6 of the specification is mystifying. She indicates that it is demonstrated that, "no derivatives of SEQ ID NO: 3 or other claimed partial peptide of SEQ ID NO: 2 comprising SEQ ID NO: 3 could bind to HLA-A24 and are recognized by T-lymphocyte." Example 6 does not even survey peptides that bind to HLA-A24. Rather, Example 6 describes an experiment that demonstrates that two particular peptide portions of SEQ ID NO: 2 bind to CTL in an HLA-A24-restricted manner, since they stimulate interferon synthesis in HLA-A24 expressing cells, but not in cells that do no express HLA-A24. (See, the bottom of page 63 of the specification.)

The specification discloses very well how to synthesize peptides of the invention and how to test them for activity in binding HLA-A24 and recognition by CTL. The Examiner cannot seriously maintain a position that the specification does not disclose how to make and use the present invention. This rejection must be withdrawn.

Rejection over prior art

Claims 2-8 and 11-15 are rejected under 35 USC § 102(b) as lacking novelty over Yang et al. (1999) in view of Uniprot database accession no. Q 15020 (providing sequence data). This rejection is traversed. Reconsideration and withdrawal thereof are requested.

Applicants have provided attached hereto a verified English translation of the priority application, thereby making their priority claim effective against intervening references. The instant rejection is thus overcome.

Claims 2-8 and 11-15 are rejected under 35 USC § 102(b) as being anticipated by Nagase et al. (1995) in view of Uniprot-7.2 accession no. Q 150202. This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested.

Nagase et al. discloses the entirety of SEQ ID NO: 2. However, the reference is silent with respect to the HLA-A24 binding activity of the protein and in particular does not direct one of ordinary skill in the art to the particular peptides recited in the present claims. See, for example, *In re Petering*, 133 USPQ 175 (CCPA 1972). Thus, the presently claimed invention is not anticipated by Nagase et al. and the instant rejection should be withdrawn.

Rejections for obviousness-type double patenting

Claims 2-5 and 11-15 are provisionally rejected under the doctrine of obviousness-type double patenting over claims 35 and 43 of copending application 10/505,955 and over claims 11, 19 and 23 of copending application 10/788,016.

The Examiner is advised that neither of these two copending applications is owned by the same entity as the present application. Therefore, the instant rejection is not appropriate, even as a provisional rejection, and must be withdrawn.

In view of the above remarks, all the claims remaining in the case as amended are submitted as defining non-obvious, patentable subject matter. Reconsideration of the rejections and allowance of the claims are respectfully requested.

If the Examiner has any questions concerning this application, the Examiner is requested to contact the undersigned at the phone number below.

Pursuant to the provisions of 37 C.F.R. 1.17 and 1.136(a), the Applicant has petitioned for an extension of three months to July 19, 2007 for the period in which to file a response to the Office Action dated January 19, 2007. The required fee has been paid in connection with the proper filing of this response.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to our Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under § 1.17; particularly, extension of time fees.

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Respectfully submitted,

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